Fig.1

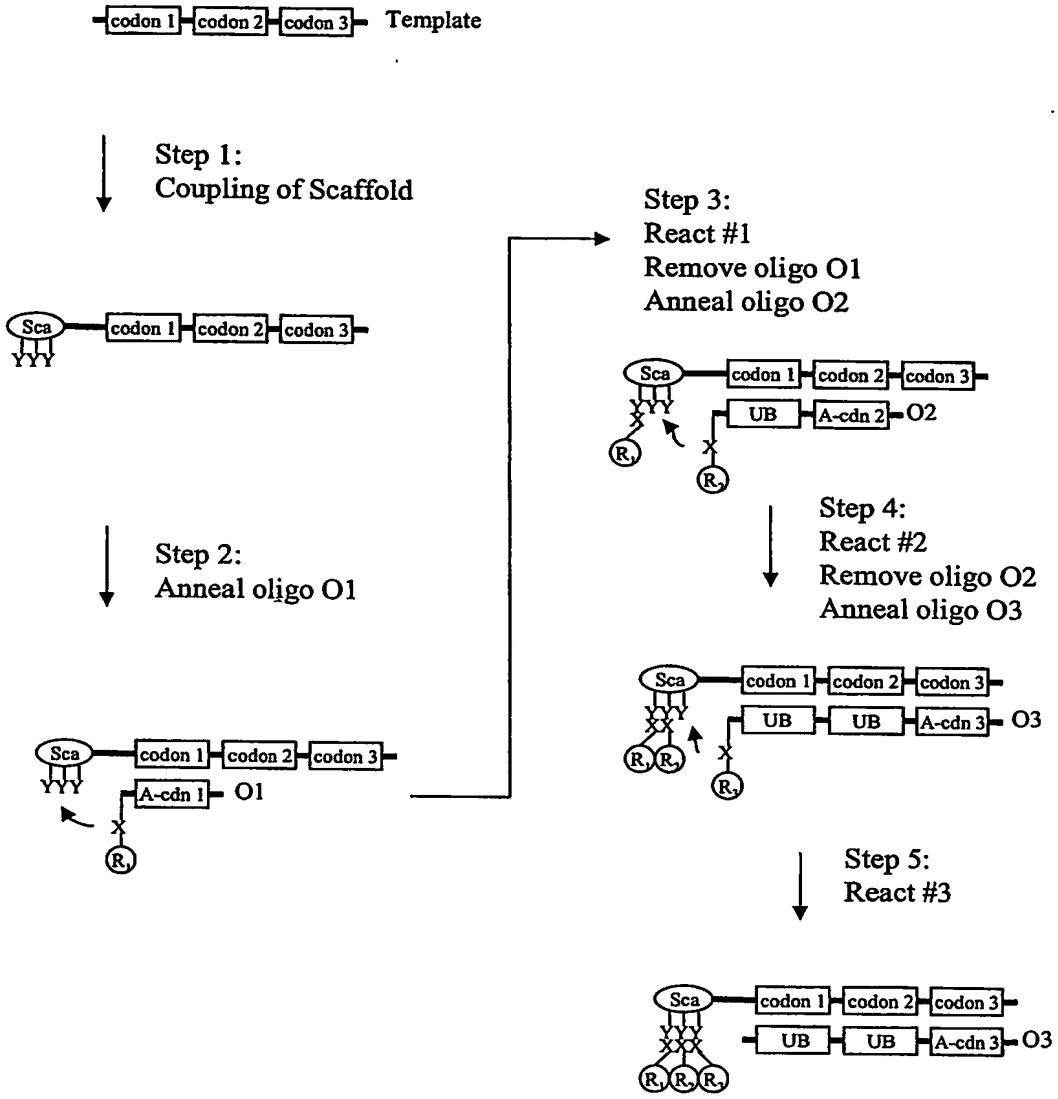

codon 1
codon 2
codon 3
Template
Step 1:
Coupling of Scaffold
Sca
Step 2:
Anneal oligo O1
A-cdn 1
O1
Step 3:
React #1
Remove oligo O1
Anneal oligo O2
UB
A-cdn 2
O2
Step 4:
React #2
Remove oligo O2
Anneal oligo O3
A-cdn 3
O3
Step 5:
React #3

Fig. 2

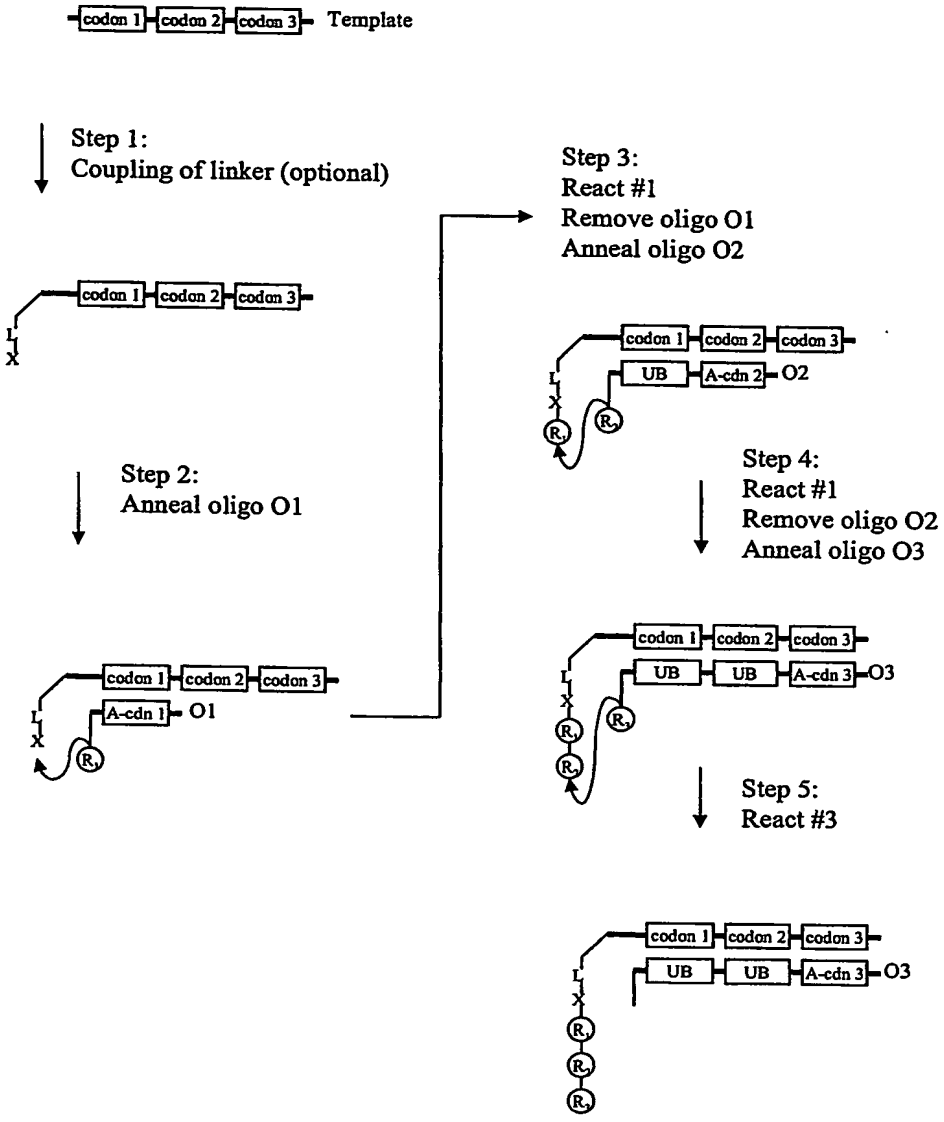

codon 1
codon 2
codon 3
Template
Step 1:
Coupling of linker (optional)
Step 2:
Anneal oligo O1
A-cdn 1
O1
Step 3:
React #1
Remove oligo O1
Anneal oligo O2
UB
A-cdn 2
O2
Step 4:
React #1
Remove oligo O2
Anneal oligo O3
UB
A-cdn 3
O3
Step 5:
React #3

Fig. 3

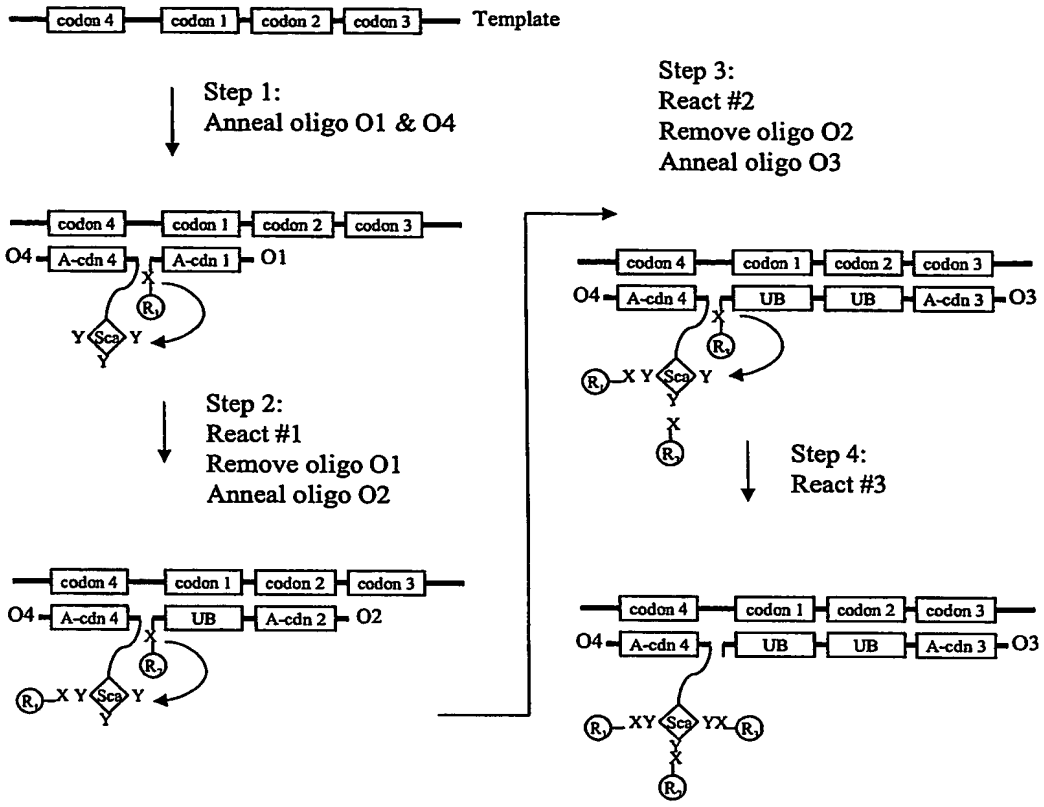

codon 4
codon 1
codon 2
codon 3
Template
Step 1:
Anneal oligo O1 & O4
O4
A-cdn 4
A-cdn 1
O1
Step 2:
React #1
Remove oligo O1
Anneal oligo O2
UB
A-cdn 2
O2
Step 3:
React #2
Remove oligo O2
Anneal oligo O3
A-cdn 3
O3
Step 4:
React #3

Fig 4

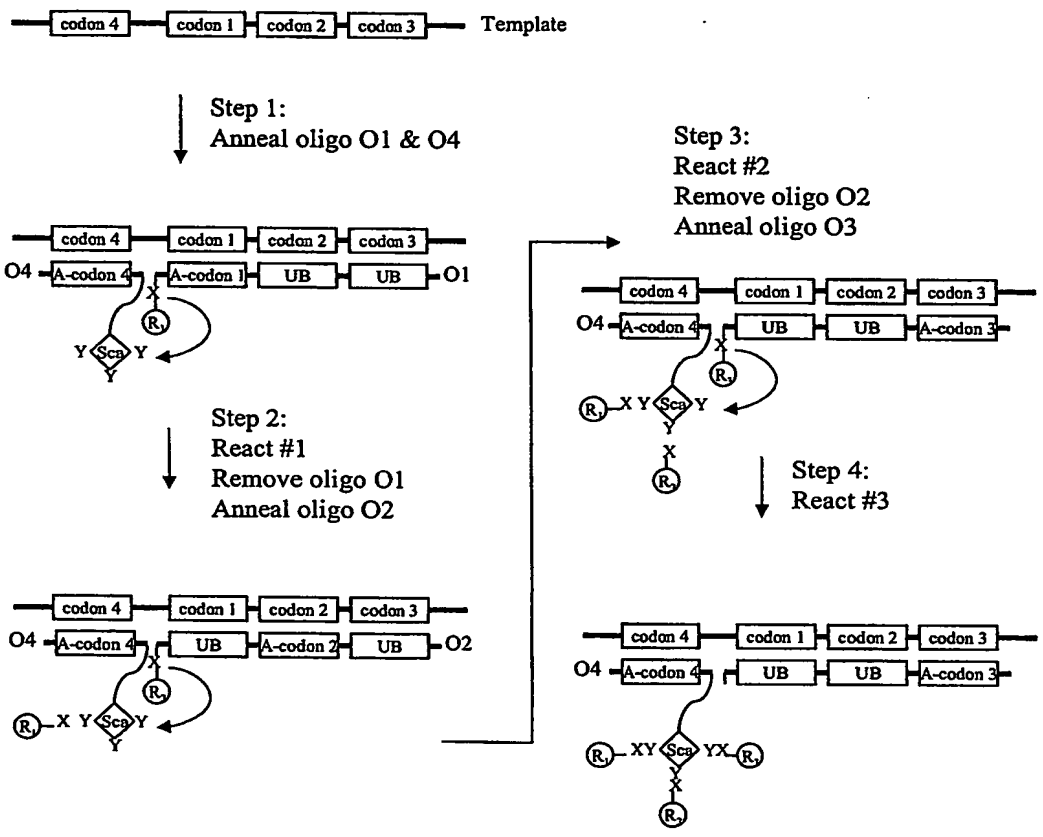

codon 4
codon 1
codon 2
codon 3
Template
Step 1:
Anneal oligo O1 & O4
O4
A-codon 4
A-codon 1
UB
UB
O1
Step 2:
React #1
Remove oligo O1
Anneal oligo O2
A-codon 2
O2
Step 3:
React #2
Remove oligo O2
Anneal oligo O3
A-codon 3
Step 4:
React #3

Fig.5

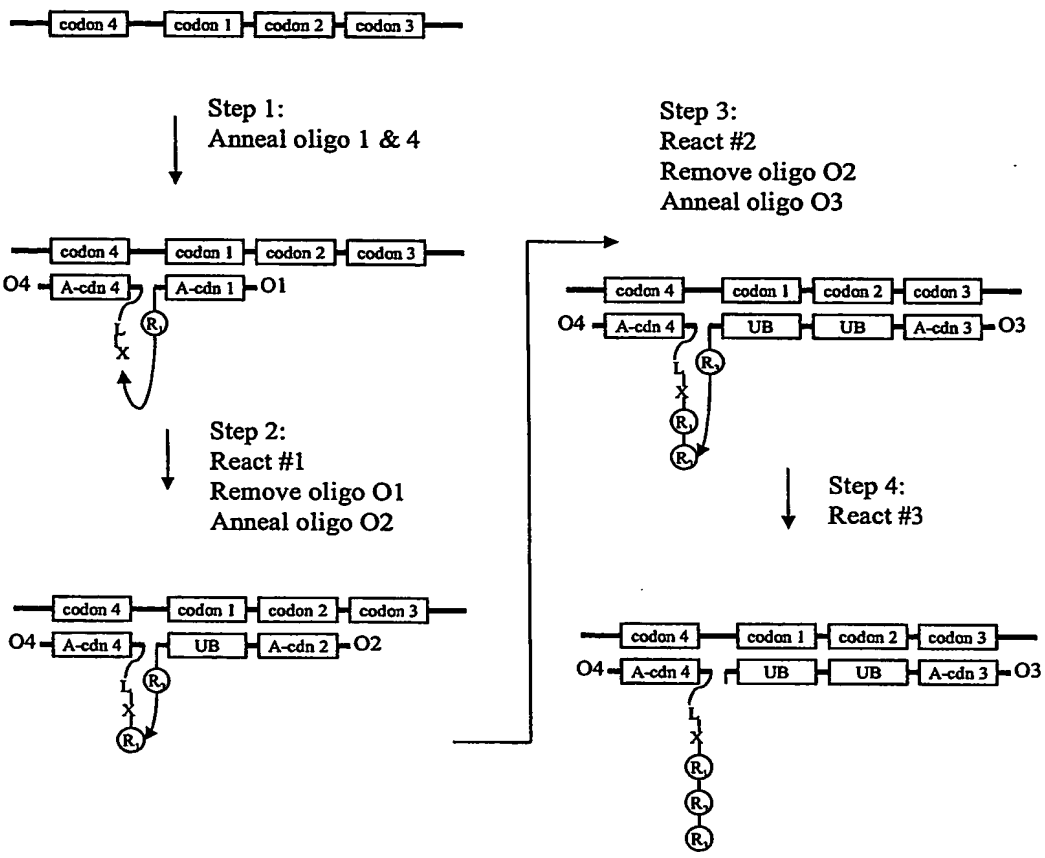

codon 4
codon 1
codon 2
codon 3
Step 1:
Anneal oligo 1 & 4
O4
A-cdn 4
A-cdn 1
O1
Step 2:
React #1
Remove oligo O1
Anneal oligo O2
UB
A-cdn 2
O2
Step 3:
React #2
Remove oligo O2
Anneal oligo O3
UB
UB
A-cdn 3
O3
Step 4:
React #3

Fig. 6

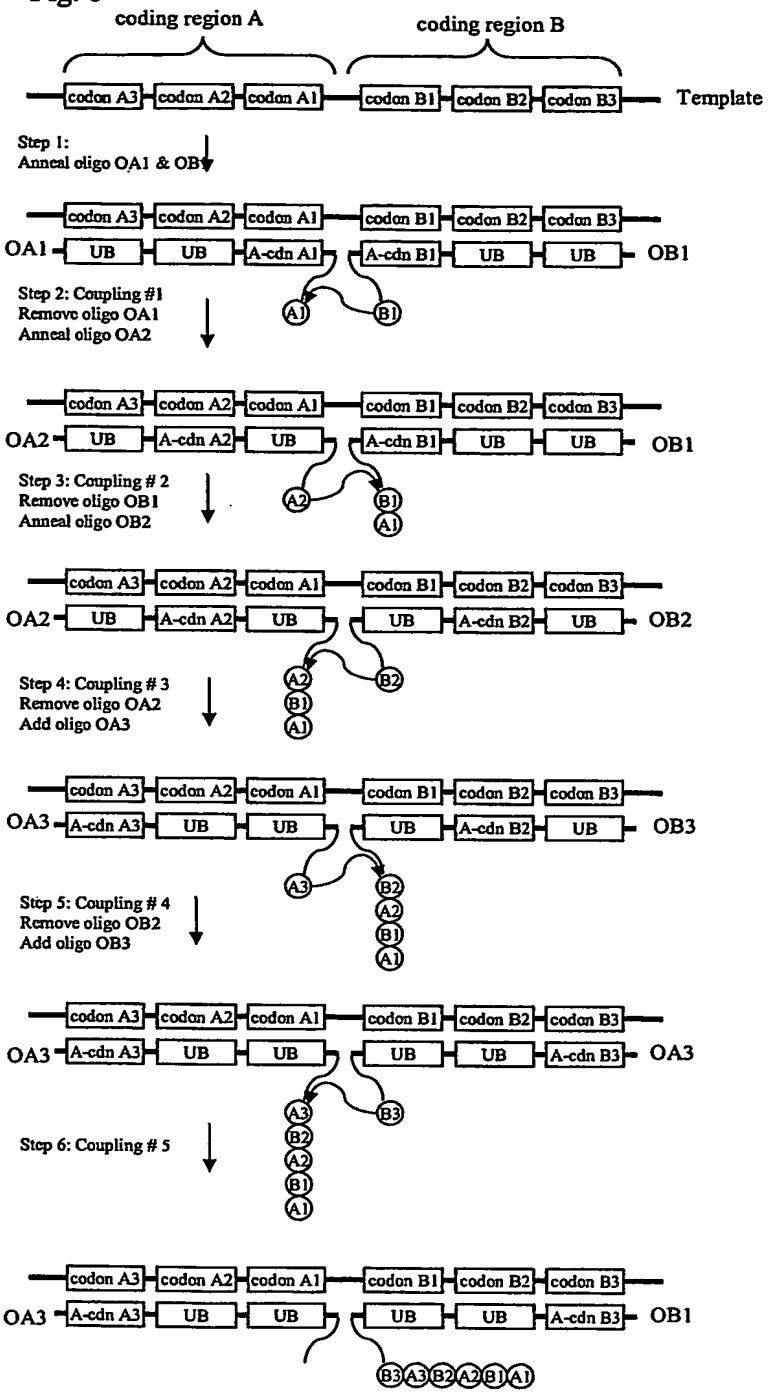

coding region A
coding region B
codon A3
codon A2
codon A1
codon B1
codon B2
codon B3
Template
Step 1:
Anneal oligo OA1 & OB1
OA1
UB
A-cdn A1
A-cdn B1
OB1
Step 2: Coupling #1
Remove oligo OA1
Anneal oligo OA2
OA2
A-cdn A2
Step 3: Coupling # 2
Remove oligo OB1
Anneal oligo OB2
OB2
Step 4: Coupling # 3
Remove oligo OA2
Add oligo OA3
OA3
A-cdn A3
OB3
Step 5: Coupling # 4
Remove oligo OB2
Add oligo OB3
A-cdn B2
A-cdn B3
Step 6: Coupling # 5

Fig. 7

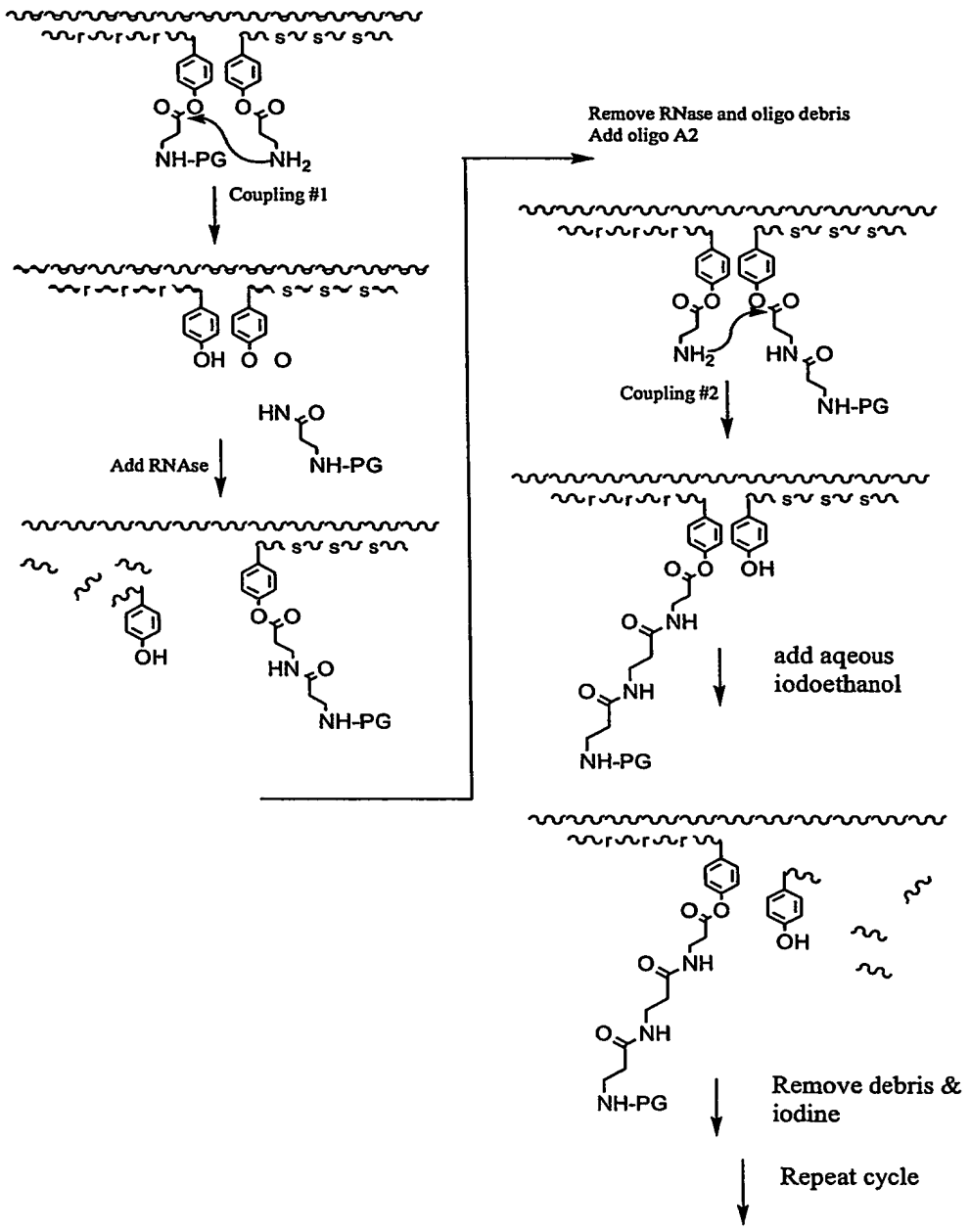
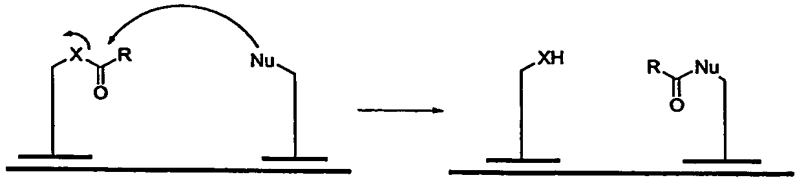

NH-PG
NH2
Coupling #1
OH
HN
NH-PG
Add RNAse
Remove RNase and oligo debris
Add oligo A2
NH2
HN
NH-PG
Coupling #2
OH
NH
NH
NH-PG
add aqeous
iodoethanol
OH
NH
NH
NH-PG
Remove debris &
iodine
Repeat cycle

Fig. 8

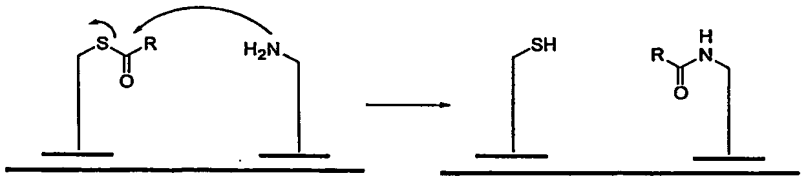
A. Acylating monomer building blocks - principle



X = O, S Nu = Oxygen-, Nitrogen-, Sulfur- and Carbon Nucleophiles

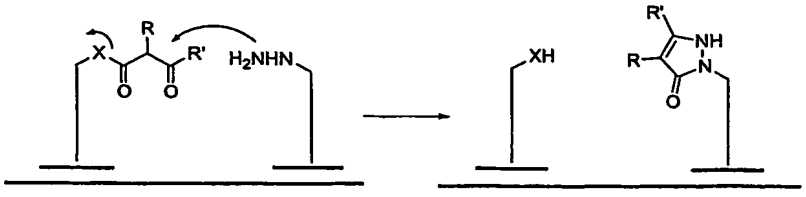
B. Acylation

Amide formation by reaction of amines with activated esters



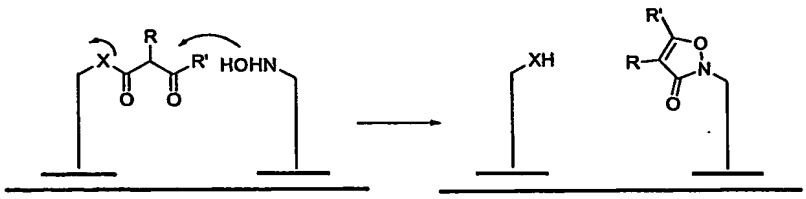
C. Acylation

Pyrazolone formation by reaction of hydrazines with β–Ketoesters



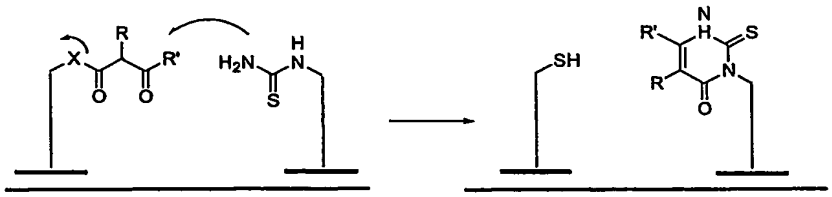
D. Acylation

Isoxazolone formation by reaction of hydroxylamines with β–Ketoesters



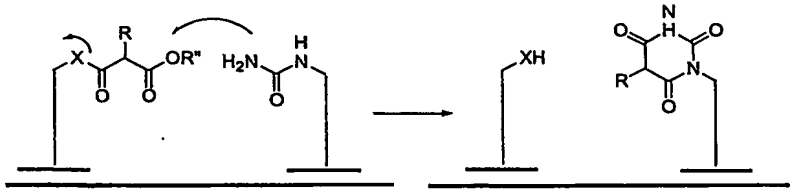
E. Acylation

Pyrimidine formation by reaction of thioureas with β–Ketoesters



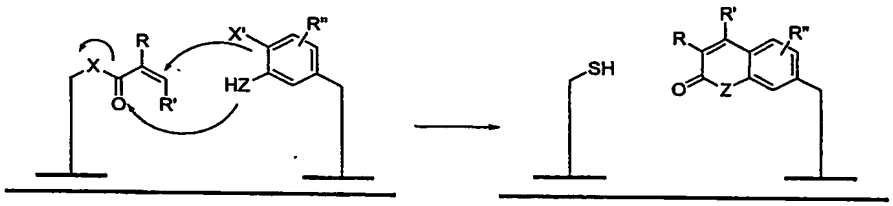
F. Acylation

Pyrimidine formation by reaction of ureas with Malonates



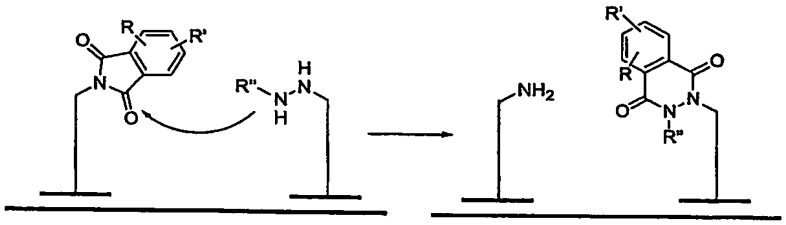
G. Acylation

Coumarine or quinolinon formation by a Heck reaction followed by a nucleophilic substitution



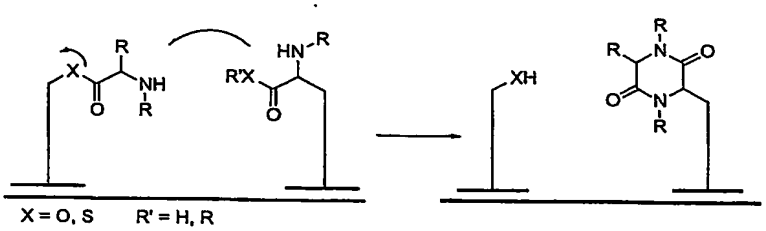
H. Acylation

Phthalhydrazide formation by reaction of Hydrazines and Phthalimides



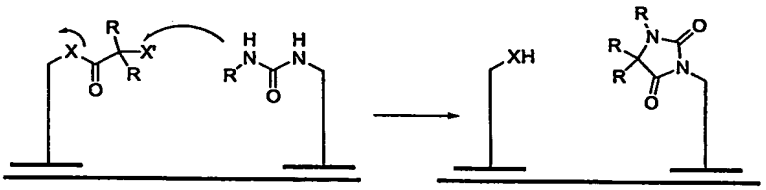
I. Acylation

Diketopiperazine formation by reaction of Amino Acid Esters



J. Acylation

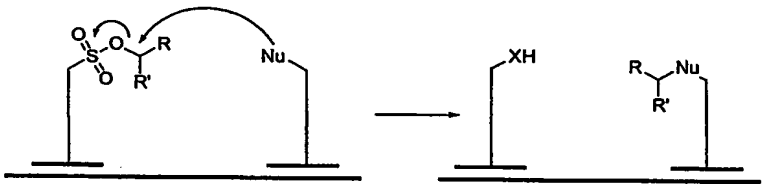
Hydantoin formation by reaction of Urea and α-substituted Esters



X = O, S X' = Hal, OTos, OMs, etc.

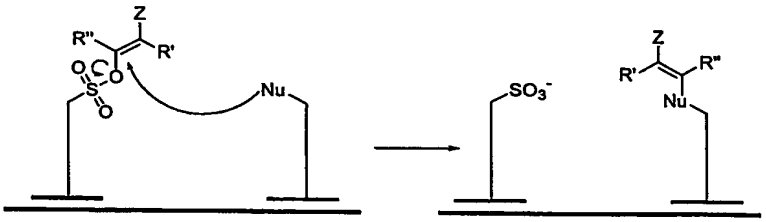
K. Alkylating monomer building blocks - principle

Alkylated compounds by reaction of Sulfonates with Nucleofiles



Nu = Oxygen- , Nitrogen- , Sulfur- and Carbon Nucleophiles

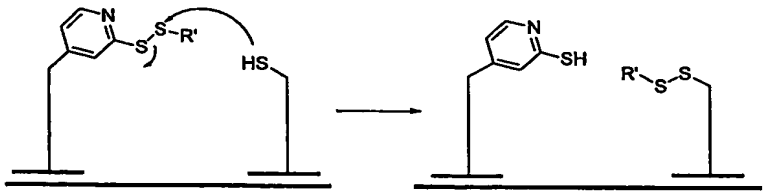
L. Vinylating monomer building blocks - principle



Z = CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F
Nu = Oxygen- , Nitrogen- , Sulfur- and Carbon Nucleophiles

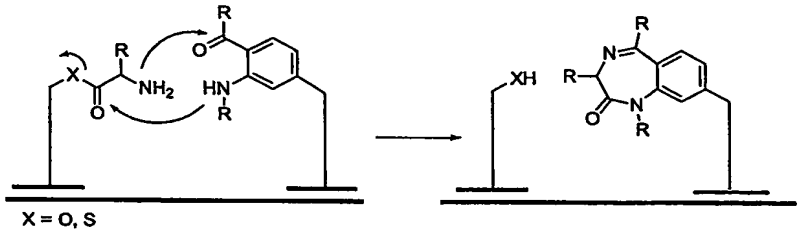
M. Heteroatom electrophiles

Disulfide formation by reaction of Pyridyl disulfide with Mercaptanes



N. Acylation

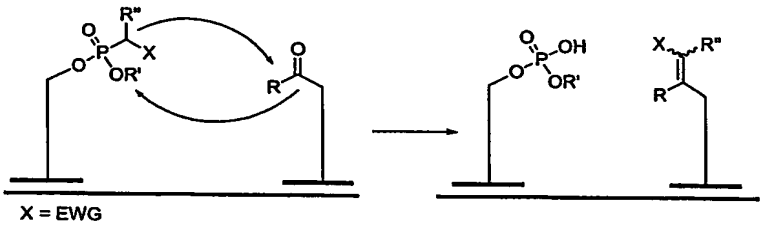
Benzodiazepinone formation by reaction of Amino Acid Esters and Amino Ketones



Addition to carbon-hetero multiple bonds

O. Wittig/Horner-Wittig-Emmons reagents

Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones

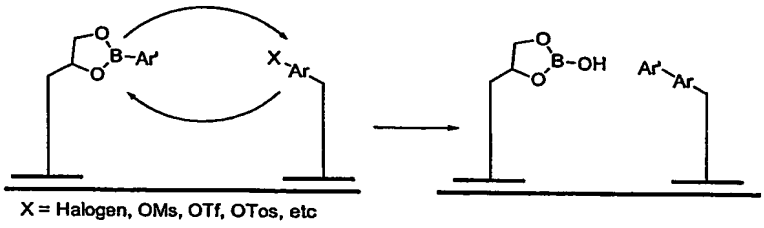


X = EWG

Transition metal catalysed reactions

P. Arylation

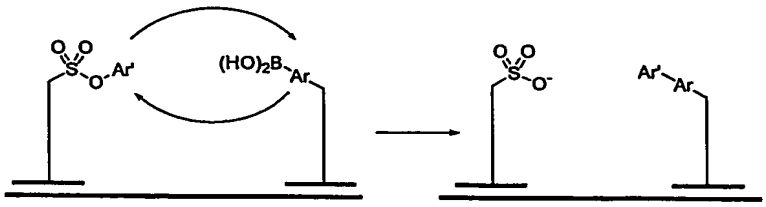
Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls



X = Halogen, OMs, OTf, OTos, etc

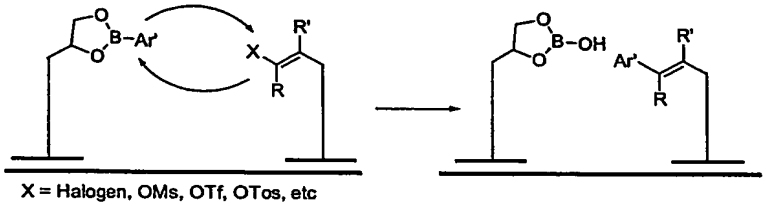
Q. Arylation

Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls



R. Arylation

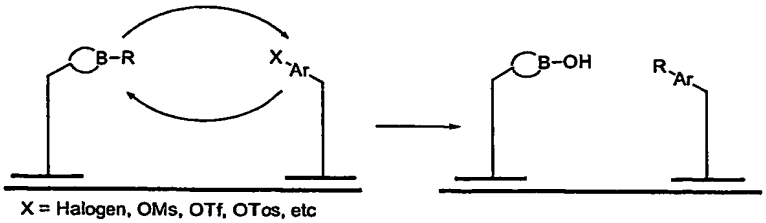
Vinylarene formation by the reaction of alkenes with Aryls or Heteroaryls



X = Halogen, OMs, OTf, OTos, etc

S. Alkylation

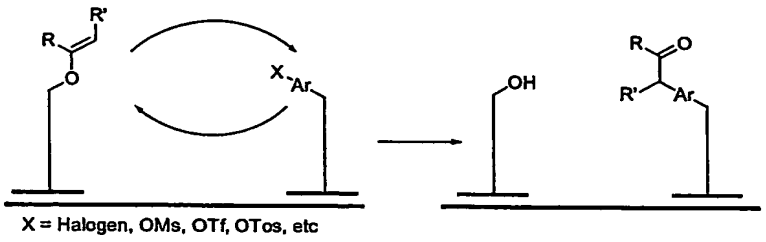
Alkylation of arenes/hetarens by the reaction with Alkyl boronates



X = Halogen, OMs, OTf, OTos, etc

T. Alkylation

Alkylation of arenas/hetarenes by reaction with enolethers

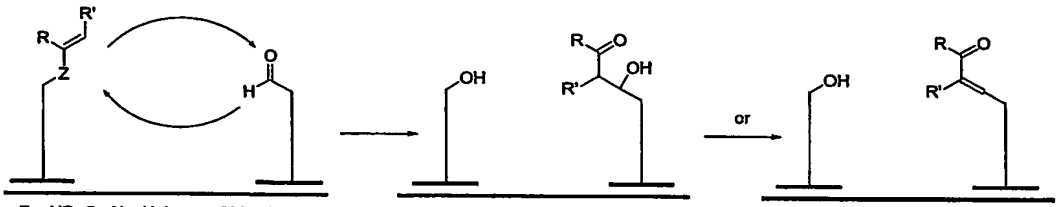


X = Halogen, OMs, OTf, OTos, etc

Nucleophilic substitution using activation of nucleophiles

U. Condensations

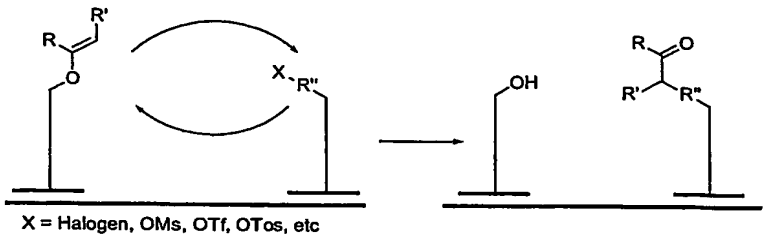
Alkylation of aldehydes with enolethers or enamines



Z = NR, O; X = Halogen, OMs, OTf, OTos, etc

V. Alkylation

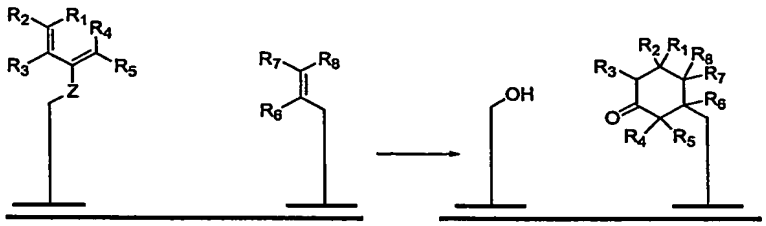
Alkylation of aliphatic halides or tosylates with enolethers or enamines



X = Halogen, OMs, OTf, OTos, etc

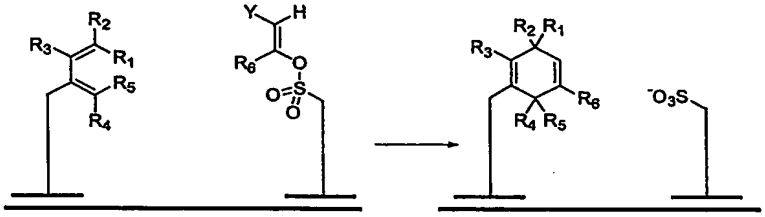
Cycloadditions

W. [2+4] Cycloadditions



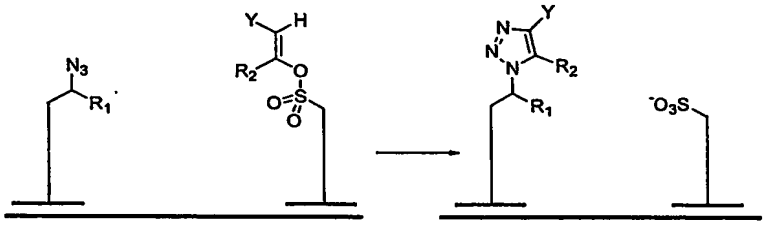
Z = O, NR

X. [2+4] Cycloadditions



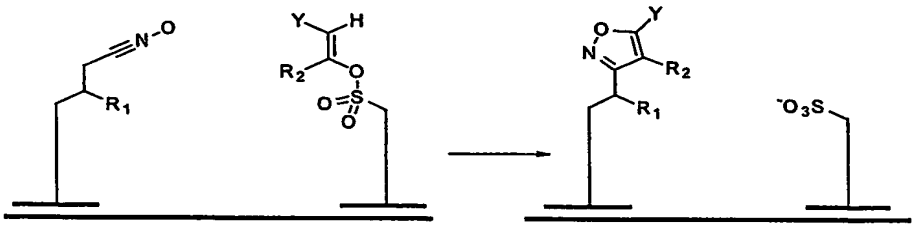
Y, CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F

Y. [3+2] Cycloadditions



Y, CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F

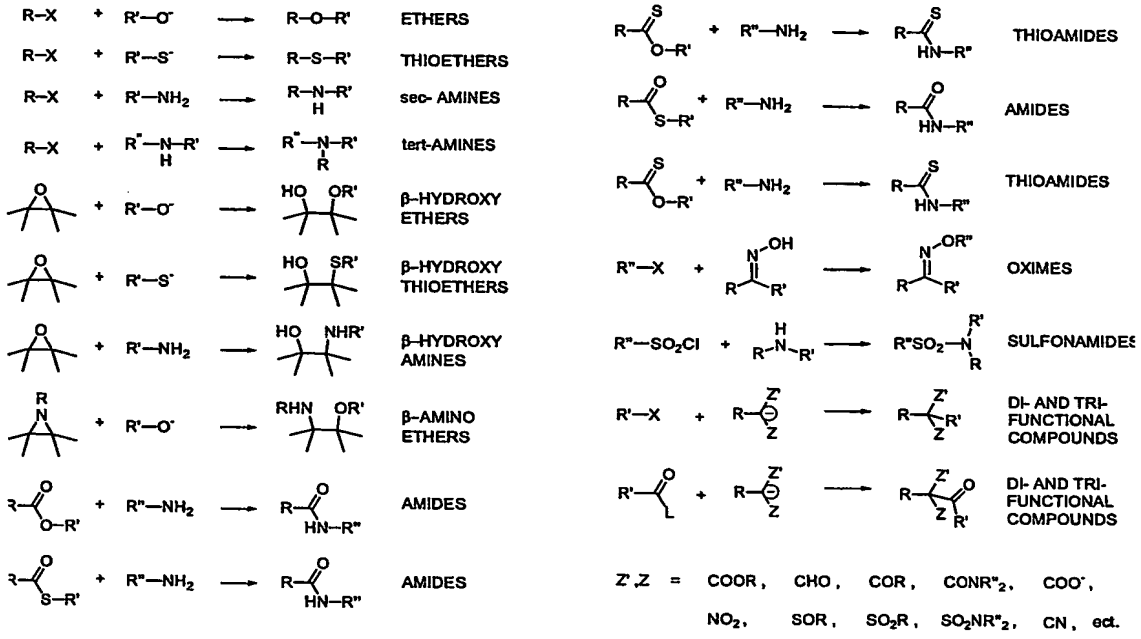
Z. [3+2] Cycloadditions



Y, CN, COOR, COR, NO_2, SO_2R, S(=O)R, SO_2NR_2, F

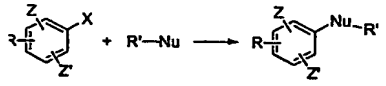
Fig. 9

Nucleophilic substitution reaction



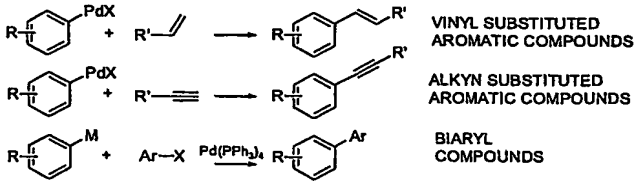
Aromatic nucleophilic substitution

SUBSTITUTED AROMATIC COMPOUNDS

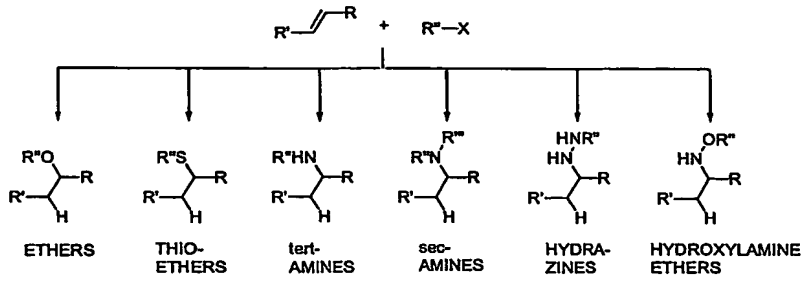


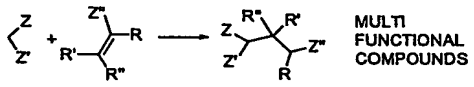
Nu = Oxygen-, Nitrogen-, Sulfur- and Carbon Nucleophiles
X = F, Cl, Br, I, OSO_2CH_3, OSO_2CF_3, OSO_2TOL, , , etc.
Z',Z = COOR, CHO, COR, $CONR"_2$, COO^-, CN, NO_2, SOR, SO_2R, $SO_2NR"_2$, , ect.

Transition metal catalysed reactions



Addition to carbon-carbon multiplebonds

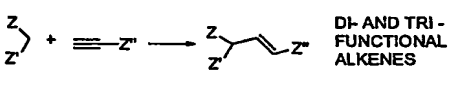




Z = H, Alkyl, Z', Ar

Z" = COOR , CHO , COR , $CONR"_2$, CN , NO_2 , SOR , SO_2R , $SO_2NR"_2$, , ect.

Z' = Z" R = R', = R", = Z

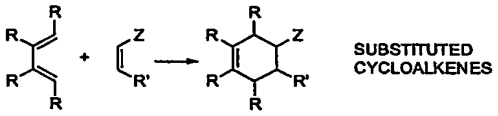


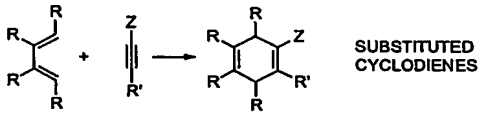
Z = H, Alkyl, Ar,

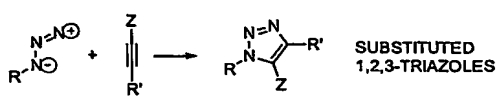
Z" = Z', Alkyl, Ar,

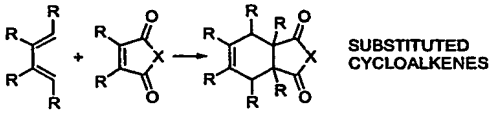
Z' = COOR, CHO, COR, $CONR"_2$, CN, NO_2, SOR, SO_2R, $SO_2NR"_2$, ect.

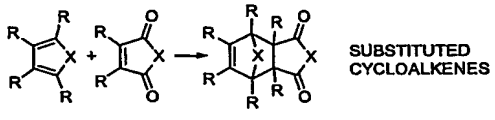
Cycloaddition to multiple bounds







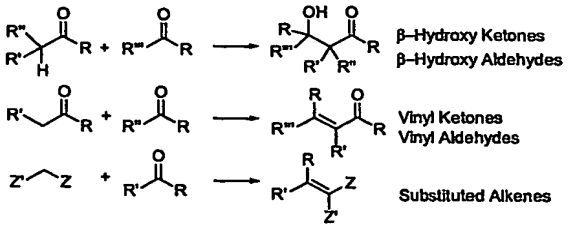


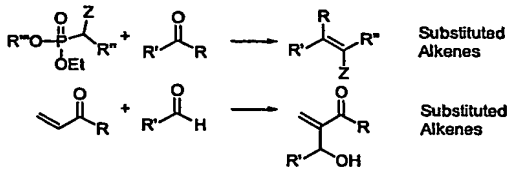


Z = COOR , CHO , COR , COOH COAr CN , NO_2 , Ar, CH_2OH, CH_2NH_2, CH_2CN, SOR, SO_2R etc.

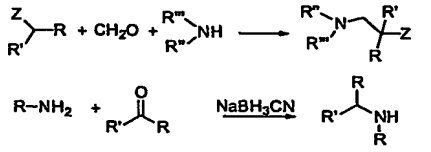
R = H, Alkyl, Ar, Z X = O, NR, CR_2, S,

Addition to carbon-hetero multiple bonds





Z, Z' = COOR, CHO, COR, $CONR''_2$, CN, NO_2, SOR, SO_2R, $SO_2NR''_2$, ect. R^n = H, Alkyl, Aryl



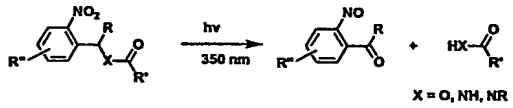
Z = COOR, CHO, COR, SOR, SO_2R, CN, NO_2, ect.

R = R', H, Alkyl, Ar,

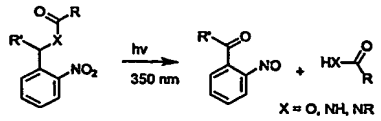
R'' = R''', H, Alkyl, COR,

Fig. 10 Cleavable Linkers

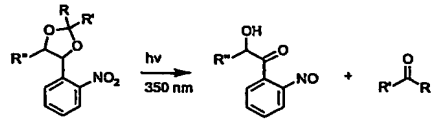
A. Linker for the formation of Ketones, Aldehydes, Amides and Acids



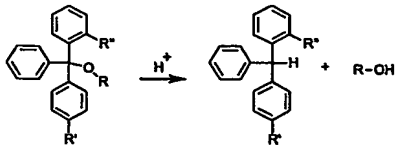
B. Linker for the formation of Ketones, Amides and Acids



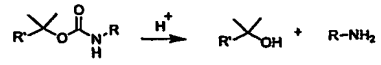
C. Linker for the formation of Aldehydes and Ketones



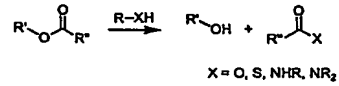
D. Linker for the formation of Alcohols and Acids



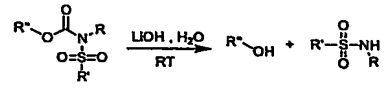
E. Linker for the formation of Amines and Alcohols



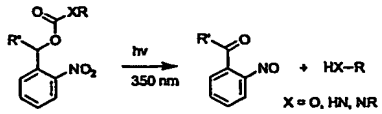
F. Linker for the formation of Esters, Thioesters , Amides, and Alcohols



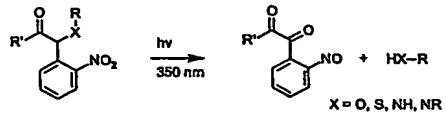
G. Linker for the formation of Sulfonamides and Alcohols



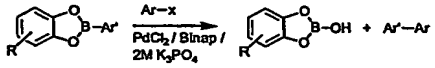
H. Linker for the formation of Ketones, Amines and Alcohols



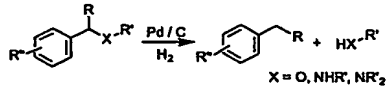
I. Linker for the formation of Ketones, Amines, Alcohols and Mercaptanes



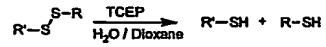
J. Linker for the formation of Biaryl and Bihetaryl



K. Linker for the formation of Benzyles, Amines, Anilins
Alcohols and Phenoles

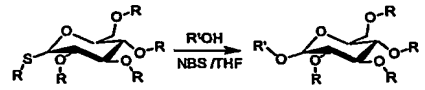


L. Linker for the formation of Mercaptanes

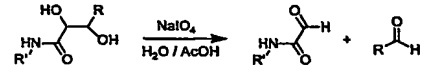


TCEP = tris(2-carboxyethyl)phosphine

M. Linker for the formation of Glycosides



N. Linker for the formation of Aldehydes and Glyoxylamides



O. Linker for the formation of Aldehydes, Ketones and
Aminoalcohols

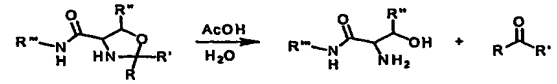
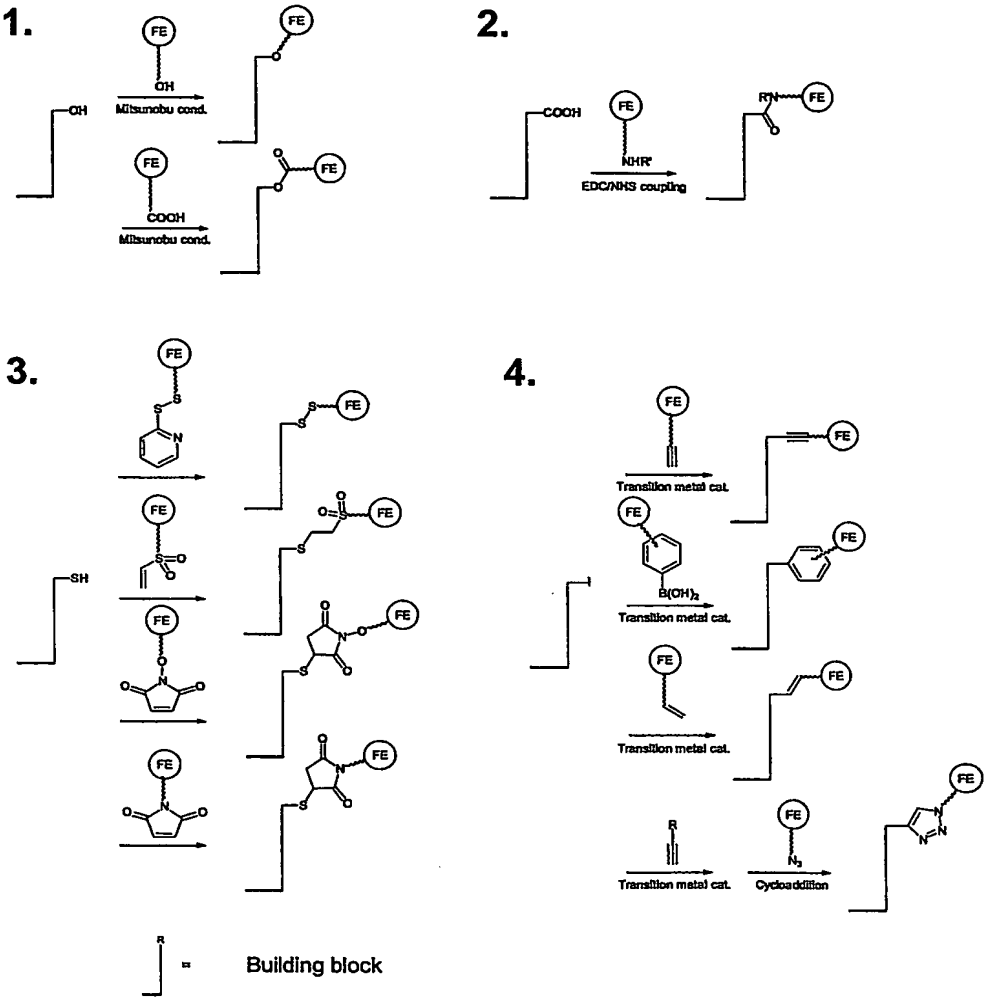


Fig. 11


1.
2.
3.
4.
FE
OH
Mitsunobu cond.
COOH
Mitsunobu cond.
COOH
NHR'
EDC/NHS coupling
SH
Transition metal cat.
B(OH)2
Transition metal cat.
Transition metal cat.
Transition metal cat.
Cycloaddition
N3
R
Building block

5.

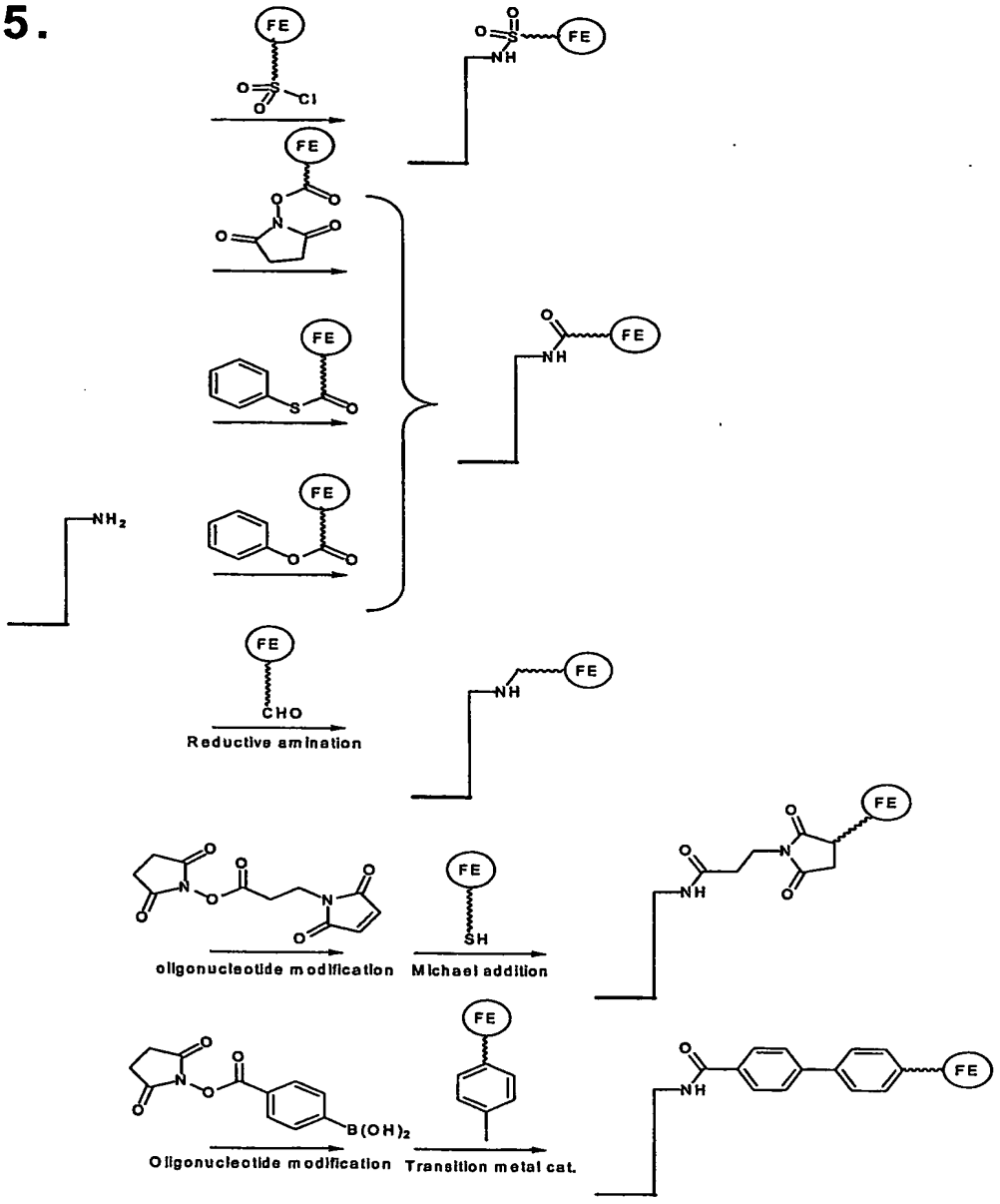
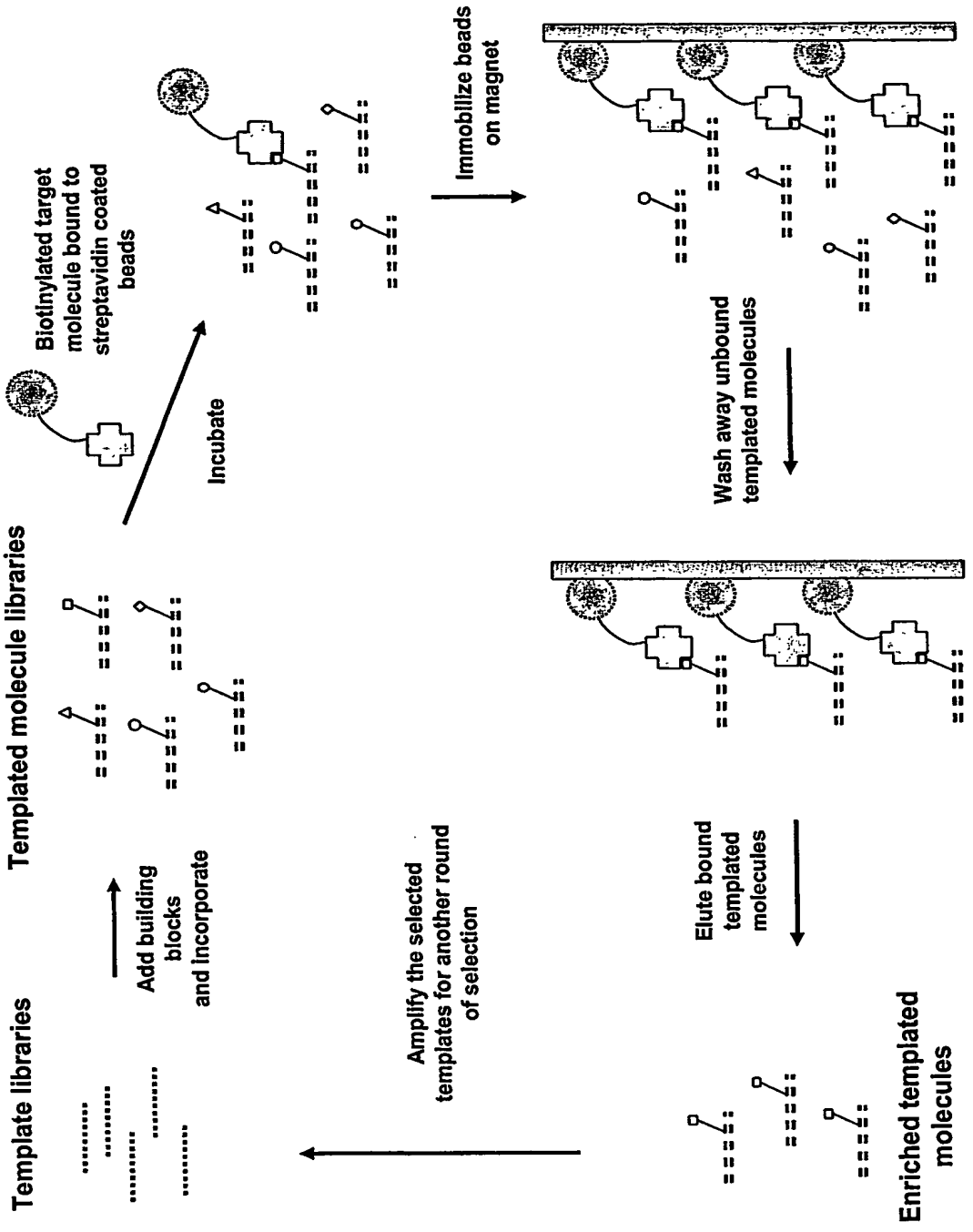

FE
Cl
NH
NH2
CHO
Reductive amination
SH
oligonucleotide modification
Michael addition
B(OH)2
Oligonucleotide modification
Transition metal cat.

Fig 12.


A typical panning protocol for selection of templated molecules
Template libraries
Add building blocks and incorporate
Templated molecule libraries
Biotinylated target molecule bound to streptavidin coated beads
Incubate
Immobilize beads on magnet
Wash away unbound templated molecules
Elute bound templated molecules
Amplify the selected templates for another round of selection
Enriched templated molecules